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CASE REPORT

Two cases of Behçet's disease with major vessel involvement

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KEYWORDS

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Abstract *Aim of the work:* We attempt here to describe 2 cases of Behçet's disease (BD) with pulmonary vascular complications.

Case presentation: Two cases of Behçet's disease with major vessel involvement are presented. The first case presented with hemoptysis and investigations revealed the presence of pulmonary artery aneurysm (PAA). The patient received pulsed methylprednisolone 1 gm/day for 3 successive days and pulse cyclophosphamide 600 mg monthly for 6 months, and oral maintenance therapy 1 mg/kg prednisolone daily. The patient's symptoms improved within 2 weeks and a follow up CT angiography after 1 year revealed normal pulmonary arteries. The second case presented with dilated tortuous veins over the chest wall and was diagnosed to have superior vena cava (SVC) obstruction. The patient was prescribed pulsed methylprednisolone 1 gm/day for 3 successive days and pulse cyclophosphamide 600 mg/month for 6 months and oral prednisolone 1 mg/kg/day maintenance therapy, in addition to, oral warfarin therapy 5 mg/day to maintain his INR at 2.5. The patient was discharged after stabilization of his condition.

Conclusion: Since a significant proportion of patients develops complications in arterial and venous vessels, vascular lesions should be included in the diagnostic criteria of BD. Challenges remain to identify those patients at risk, to understand the cause and best treatment of thrombosis in these patients, and to develop well tolerated and effective therapies to arrest or reverse the course of vasculitis in BD.

1. Introduction

Behçet's disease (BD) is a chronic, relapsing, multisystemic disorder characterized by recurrent oro-genital ulcers and ocular inflammation with cutaneous, musculoskeletal, vascular and nervous system manifestations [1]. The etio-pathogenesis of the disease remains obscure, although genetic predisposition, environmental factors and immunological abnormalities have been implicated [2,3]. BD has a worldwide distribution; however, it is mainly seen in Far East and Middle East countries.

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HLA-B51 has been suggested to be associated with the risk of BD [4]. The age of disease onset is usually in the second or third decade of life with almost equal male to female ratio. However, the disease is more severe in men and in those with onset before 25 years of age [5].

The diagnosis of BD is made on the basis of the criteria proposed by the International Study Group (ISG) for Behçet disease in 1990 [6]. According to the criteria, recurrent oral ulceration must be present along with at least 2 of the following: recurrent genital ulceration, eye lesions, skin lesions and a positive pathergy test. Vasculitis is thought to underlie many of the clinical manifestations of BD. The vasculitis of BD is distinctive because of involvement of both arteries and veins of all sizes [7]. Large vessel vasculitis is seen in up to 40% of the patients and it was proposed to be one of the diagnostic criteria of the disease [8,9]. Lower extremity vein thrombosis is the most frequent manifestation of vascular involvement, followed by vena cava thrombosis, pulmonary artery aneurysms (PAA), Budd–Chiari syndrome, peripheral artery aneurysms, dural sinus thrombosis and abdominal aorta aneurysms [10]. Venous system involvement is more common than arterial system involvement; however, rupture of an arterial aneurysm remains a major cause of mortality related to BD [11].

We attempt here to describe 2 cases of BD with pulmonary vascular complications. It is important to recognize these patients early as their prognosis is less favorable and they are candidates for more aggressive treatment.

2. Case 1

A 37 year old male patient, occasional smoker, presented complaining of high grade fever of 5 months duration associated with rigors and sweating with no diurnal variation, 3 months later the patient experienced recurrent attacks of hemoptysis associated with dyspnea with no cough or chest pain. During this period he developed recurrent oral and genital ulcers, with no ocular manifestations or skin rash. The patient sought medical advice and was diagnosed to have chest infection. He received antibiotics with no improvement. The patient was then referred to an expert rheumatologist. On examination the patient was conscious and alert, his blood pressure was 140/80, pulse was regular with intact peripheral pulsation and temperature was 38.3 °C. Systemic examination revealed no abnormality. There were oral and genital ulcers. Pathergy test was negative and ophthalmologic examination was free. Laboratory analysis showed: white blood count was $10.08 \times 10^3/\mu L$, hemoglobin was 11.0 g/dL, hematocrit was 32.1% and erythrocyte sedimentation rate was 62 mm/h. The possibility of BD was raised. Chest X-ray showed an opacity in the inferior lobe of the left lung and CT pulmonary angiography showed aneurismal dilatation of the inferior lingular branch of the left pulmonary artery (Fig. 1).

The patient received pulsed methylprednisolone 1 gm/day for 3 successive days and pulse cyclophosphamide 600 mg monthly for 6 months, and oral maintenance therapy 1 mg/kg prednisolone daily. The patient's symptoms improved within 2 weeks and a follow up CT angiography after 1 year revealed normal pulmonary arteries. The patient is under follow up schedule (Fig. 2).

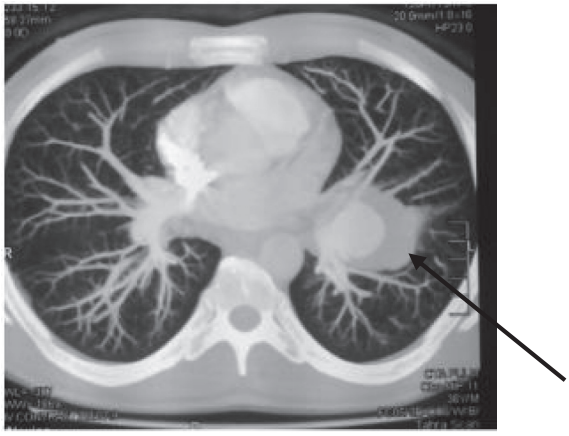

Figure 1 CT pulmonary angiography showing aneurismal dilatation of the inferior lingular branch of the left pulmonary artery (arrow), with partial thickness of its lumen.

Figure 2 Follow up CT pulmonary angiography after 1 year, showing complete disappearance of the pulmonary aneurysm (arrow).

3. Case 2

A 37 year old male, heavy cigarette smoker, presented complaining of painful swelling in the left arm, edema of the face and eye lids of 8 months duration. This was associated with the development of dilated veins on the front of the chest and abdomen. During the past 3 years the patient gave a history of recurrent painful oral ulcers and multiple painful papules on the scrotum and inner aspects of the upper parts of both thighs which then rupture leaving painful ulcers. He gave no history of ocular manifestations. On examination the patient was conscious and alert. His blood pressure was 130/80, pulse was regular with intact peripheral pulsations and temperature was 37 °C. He had a puffy face and eye lids, congested non pulsating neck veins, dilated veins on the front and back of the chest and left shoulder filling from above downwards with no redness or tenderness (Fig. 3). He also had white scars on the scrotum and crusted lesions on the inner sides of the upper thighs. Systemic examination was free. Ophthalmological examination was free and pathergy test was negative. Laboratory tests showed white blood count was $8.2 \times 10^3/\mu L$, hemoglobin was 12.0 g/dL, hematocrit was 32.1% and

Figure 3 Dilated veins on the front of the chest.

erythrocyte sedimentation rate was 100 mm/h. The patient was diagnosed to have Behçet's disease. CT pulmonary & aortic angiography were ordered which showed partial superior vena cava (SVC) obliteration at the level of the aortic arch with proximal and distal recanalization (Fig. 4). Numerous mediastinal and to a lesser degree chest wall collaterals were noted.

The patient was prescribed pulsed methylprednisolone 1 gm/day for 3 successive days and pulse cyclophosphamide 600 mg/month for 6 months and oral prednisolone 1 mg/kg/day maintenance therapy, in addition to, oral warfarin therapy 5 mg/day to maintain his INR at 2.5. The patient was discharged after stabilization of his condition; however he did not follow his condition in our hospital.

4. Discussion

We report 2 rare cases of BD with pulmonary vascular involvement. The first patient presented with pulmonary arterial aneurysm secondary to vasculitis, fulfilling the BD criteria.

Pulmonary artery aneurysms (PAA) are observed in less than 5% of patients with BD [11] and are the most lethal complication of the disease [10]. As in our patient, PAA usually present with hemoptysis, accompanied by chest pain, cough and dyspnea in varying degrees. Rupture of an aneurysm with erosion into a bronchus has been suggested as an explanation for the hemoptysis [12]. Fever, fatigue and an increased acute phase response characterize the early stages of these aneurysms [7]. The presence of hemoptysis may lead to the misdiagnosis of tuberculosis. Considering the rarity of pulmonary emboli in Behçet's disease, hemoptysis should be viewed with a very high index of suspicion for PAA [7]. PAA aneurysms, usually bilateral, develop preferentially in the large and medium sized pulmonary arteries [12]. Thrombi within the aneurysms and coexisting venous thrombosis are usually present (81%). Intracardiac thrombus formation and arterial disease in other sites may further complicate the clinical picture [12,13].

A plain chest radiograph usually shows round hilar or peripheral opacities, frequently multiple and bilateral. Spiral CT scan of the lungs shows the aneurysms and the accompanying thromboses in most of the cases and may also be used in monitoring therapy. Multislice CT and MR angiography are other imaging alternatives [14,15].

The mechanism of vascular lesions remains unknown. It is commonly believed that complicated interactions among T cells, neutrophils, and antigen-presenting cells are implicated in the immunity-related pathogenesis of BD. Inflammatory obliterative endarteritis of the vasa vasorum, endothelial cell swelling and mononuclear perivascular infiltration cause destruction of media, arterial wall weakening and aneurysm formation [16].

Pulmonary artery aneurysms (PAA) carry a bad prognosis in patients with BD; Hamuryudan et al. reported that 12 of 24 patients (50%) died after an average of 10 months after the onset of hemoptysis [17]. A variety of treatment modalities, such as surgery, anticoagulation, embolization, and more effectively of them all immunosuppression especially with cyclophosphamide and high dose steroids have been used in the management of PAA with limited success [7,10,18].

In a study of 534 patients with BD, only 8 suffered from PAA, but 6 of these died despite immunosuppressive treatment or surgery [6]. However, a more recent study by Hamuryudan et al., presenting the data of 26 patients having BD with PAA, showed an improved survival rate of 62%; secondary to prompt diagnosis of PAA and early commencement of long term immunosuppression with cyclophosphamide and steroids [12].

In one case report, a 39-year-old man with BD presented with hemoptysis with computed tomography and magnetic resonance angiography revealing multiple, bilateral PAAs; a

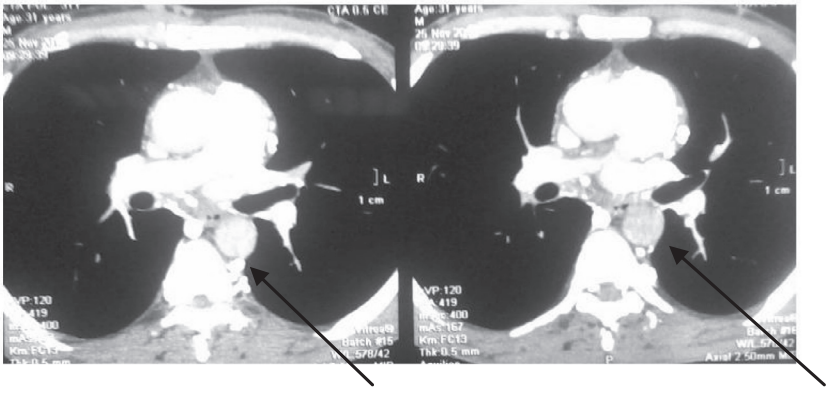

Figure 4 CT pulmonary and aortic angiography showing partial SVC obliteration at the level of aortic arch with proximal and distal recanalization.

course of cyclophosphamide and corticosteroid therapy resulted in complete resolution of his radiologic findings [19].

Our patient was treated with methylprednisolone and cyclophosphamide combination therapy followed by prednisolone maintenance therapy. We have observed complete clinical and radiological improvement within 1 year.

Our second patient presented with the SVC syndrome caused by obliteration of the SVC lumen. Superior vena cava thrombosis is a rare but easily identified manifestation of BD. With adequate collateral vessels, patients may tolerate chronic caval occlusion for many years, but deaths have been reported as a result of extensive thrombosis, treatment, hemoptysis, or other vascular causes including, very rarely, pulmonary embolus [20]. Superior vena caval occlusion leads to cyanosis and swelling of the face and upper extremities with congested non pulsating jugular veins [21].

The management of venous disease in BD is controversial. Some groups use routine anticoagulation whereas others utilize immunosuppressives. A combination of the two approaches is also occasionally advised [22]. The absence of embolization, the lack of a consistent coagulation abnormality [23,24] coupled with tightly adherent thrombi to the vessel wall suggesting an inflammatory pathology [25] favor the use of immunosuppressives but controlled data are lacking.

Our patient with PAA did not fulfill the ISG criteria for the diagnosis of BD. Several cases of BD who did not fulfill the ISG criteria have been reported [26,27]. It has been suggested that separate diagnostic criteria be established for BD with vascular involvement [28]. Since a significant proportion of patients develops complications in arterial and venous vessels, vascular lesions should be included in the diagnostic criteria of BD. Challenges remain to identify those patients at risk, to understand the cause and best treatment of thrombosis in these patients, and to develop well tolerated and effective therapies to arrest or reverse the course of vasculitis in BD.

Conflict of interest

None.

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